## REMARKS/ARGUMENTS

### *I. Status of the Claims*

Claims 1-8 and 10-30 are pending. Claim 9 is cancelled. Claims 16-23 have been withdrawn. Claims 30-36 are new. Claims 1-8, 10-15 and 24-36 are under consideration. Claim 1 is amended.

### *II. Support for Amendments to the Claims*

Applicants have amended claim 1 to replace the term "treating a subject with cancer" with "localizing an antibody-metal chelate complex to a desired tissue by administering a macrocyclic metal chelate". Support for this amendment is provided in paragraph 249 of the specification.

### *III. Support for the New Claim*

Support for new claim 30 is provided in paragraph 247 of the specification.

Support for new claim 31 is provided in paragraphs 93, 243 and 251 of the specification, as well as in originally filed claim 16.

Support for new claim 32 is provided in paragraphs 247-257 of the specification.

### *IV. Claim Rejections Under 35 U.S.C. § 112, first paragraph, written description:*

Claims 1-4, 10-15 and claims 28-29 are rejected on pages 2-6 of the Office Action under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. According to the Office Action,

> [T]he claims are inclusive of a genus of antibodies comprising an antigen recognition domain that recognizes a genus of macrocyclic metal chelate and targeting moiety that binds specifically to cancer cells. Thus, the claims are broadly drawn to antibodies defined solely by their antigen recognition domain for any macrocyclic metal chelate, which is simply a wish to know the identity of any material with that binding property. However, the written description in this case only sets forth an antibody referred to as 2D12.5 comprising an antigen recognition domain that recognizes

> one sub genus of macrocyclic metal chelate represented in claim 6 and a targeting moiety that binds specifically to a cancer cell.

Applicants traverse the rejection. In particular, Applicants direct the Examiner's attention to paragraph [0108] of the published application which discloses:

> The present invention provides for the expression of nucleic acids corresponding to the wild-type of essentially any antibody that can be raised against a metal chelate, and the modification of that antibody to include a reactive site. In a preferred embodiment, the Fab heavy chain of the wild-type antibody is the amino acid sequence set forth in SEQ ID NO.: 5 (FIG. 1) or is encoded by the nucleic acid sequence set forth in SEQ ID NO.: 16 (FIG. 3). In another preferred embodiment, the light-chain of the wild-type antibody is the amino acid sequence set forth in SEQ ID NO.: 1 (FIG. 1) or is encoded by the nucleic acid sequence set forth in SEQ ID NO.: 25 (FIG. 5). In yet another preferred embodiment, the invention provides a mutant of the light chain of 2D12.5 in which is substituted by C and that has the amino acid sequence set forth in SEQ ID NO.: 23 (FIG. 4), or is encoded by the nucleic acid sequence set forth in SEQ ID NO.: 26 (FIG. 5). In yet another preferred embodiment, the invention provides a mutant of the heavy-chain of 2D12.5 in which N-87 is replaced by D and that has the amino acid sequence set forth in SEQ ID NO.: 11 (FIG. 2) or is encoded by the nucleic acid sequence set forth in SEQ ID NO.: 17 (FIG. 3). In yet another preferred embodiment, the invention provides a mutant of the heavy-chain of 2D12.5 in which N-87 is replaced by D and G-53 is replaced by C, and that has the amino acid sequence set forth in SEQ ID NO.: 12 (FIG. 2) or is encoded by the nucleic acid sequence set forth in SEQ ID NO.: 18 (FIG. 3). In yet another preferred embodiment, the invention provides a mutant of the heavy-chain of 2D12.5 in which N-87 is replaced by D and G-54 is replaced by C, and that has the amino acid sequence set forth in SEQ ID NO.: 13 (FIG. 2) or is encoded by the nucleic acid sequence set forth in SEQ ID NO.: 19 (FIG. 3). In yet another preferred embodiment, the invention provides a mutant of the heavy-chain of 2D12.5 in which N-87 is replaced by D and G-55 is replaced by C, and that has the amino acid sequence set forth in SEQ ID NO.: 14 (FIG. 2) or is encoded by the nucleic acid sequence set forth in SEQ ID NO.: 20 (FIG. 3).

(See published application at paragraph [0108]).

Thus, Applicants respectfully submit that they have in fact provided a number of species to adequately support the claimed genus. Applicants respectfully submit that claims 1-4, 10-15 and 28-29 comply with the written description requirement. Applicants therefore respectfully request withdrawal of the rejection of claims 1-4, 10-15 and 28-29 under 35 U.S.C. § 112, first paragraph.

*V. Claim Rejections Under 35 U.S.C. § 112, first paragraph, enablement:*

Claims 1-8, 10-15 and 24-29 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. According to the Office Action,

> the specification and prior art, while being enabling for a method of treating cancer in a subject comprising administering an antibody comprising an antigen recognition domain that recognizes a macrocyclic metal chelate such as DOTA, wherein said antibody comprises a targeting moiety, anti-CEA, that binds to a cancer cell by binding with a cell surface antigen; and administering to said subject a metal chelate, allegedly does not reasonably provide enablement for a method of treating any cancer in a subject comprising administering any and/ or all antibodies comprising an antigen recognition domain that recognizes a macrocyclic metal chelate, wherein said antibody comprises any and /or all targeting moieties which bind to a cancer cell by binding to any and / or all cell surface receptors and cell surface antigens; and a macrocyclic metal chelate.

Without acceding to the Examiner's interpretation concerning enablement, Applicants have amended the claims in order to more clearly point out the presently claimed embodiments. Since the claims no longer recite a method of treating cancer, the current enablement rejection regarding cancer is moot. Therefore, Applicants respectfully request withdrawal of this rejection.

Claims 1-8, 10-15, 24-36 now recite a method of localizing an antibody-metal chelate complex to a desired tissue. These claims are enabled by the specification, especially paragraphs 13-28 and paragraphs 247-257. Of particular note are the recitations of dosages, routes of administration etc. which are found in the scientific articles which are incorporated by reference in paragraph 251 of the specification. Conditions for localizing antibody-metal

chelates in mice are provided in the following scientific articles: Goodwin *et al.*, U.S. Pat. No. 4,863,713; Goodwin *et al.*, *J. Nucl. Med.* 29: 226 (1988); Hnatowich *et al.*, *J. Nucl. Med.* 28: 1294 (1987); Klibanov *et al.*, *J. Nucl. Med.* 29: 1951 (1988); Sinitsyn *et al.*, *J. Nucl. Med.* 30: 66 (1989); Schechter *et al.*, Int. J. Cancer 48:167 (1991); and Paganelli et al., *Nucl. Med. Commun.* 12: 211 (1991). Conditions for localizing antibody-metal chelates in humans are provided in the following scientific articles: Kalofonos *et al.*, *J. Nucl. Med.* 31: 1791 (1990); Paganelli *et al.*, *Cancer Res.* 51:5960 (1991); and Paganelli et al., *Nucl. Med. Commun.* 12: 211 (1991). With the conditions provided in these scientific articles, one of skill in the art would be able to practice the claimed invention without undue experimentation. Therefore, claims 1-8, 10-15 and 24-36 are enabled. In addition, the Examiner states on page 7, first paragraph of the Office Action dated March 24, 2006 that the content of claim 36 is enabled.

***VI. Claim Rejections Under 35 U.S.C. § 102***

To maintain a *prima facie* case of anticipation, the Examiner must demonstrate that each and every element as set forth in the claim is either expressly found or is inherently described in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the ...claim. See MPEP § 2131. Applicants submit that each element of the claims now pending has not been identified in the art presently of record. Therefore, Applicants respectfully traverse the following rejections.

*Under § 102(b) over Hansen II*

Claims 1-8, 10-15 and 24-29 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Hansen, *et al.* (WO 99/66951) ("Hansen II"). Hansen II is cited by the Examiner for teaching a method of treating cancer in a subject by, among other things, administering an antibody that recognizes a targetable conjugate.

Hansen II is similar to the Hansen reference (US 2002/0006379, 1/17/2002) cited in a previous Office Action. As in the first Hansen reference, the targetable conjugate in Hansen II is a DOTA chelate with a peptide side chain. While Hansen II's antibody recognizes a targetable conjugate, the antibody is only recognizing a peptide sequence on the conjugate, and not the macrocyclic metal chelate itself. Therefore, any chelate, or any other molecule, could

replace the macrocyclic metal chelate on Hansen II's targetable conjugate and binding would be the same, so long as the peptide side chain is not manipulated or interfered with. Therefore, Hansen II is missing Applicants' element of an antibody that "recognizes a macrocyclic metal chelate". Since all the elements of the Applicants' invention are not present in Hansen II, the anticipation rejection cannot be maintained.

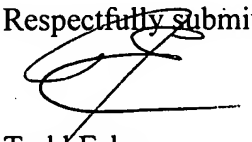
Applicants respectfully request the withdrawal of these rejections.

## CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-442-1000.

Respectfully submitted,



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